# *Acid Base Balance*

- ***Acid:*** A molecule that contributes $H^+$ to solution, i.e. proton donor. According to the degree of dissociation it may be:-

a) Strong Acid: dissociation is complete:

$$\mathbf{HCl} \xrightarrow{\mathbf{100\%}} H^+ + \mathbf{Cl^-}$$

b) Weak Acid: dissociation is weak:

$$H_2\mathbf{CO_3} \underset{\mathbf{99\%}}{\overset{\mathbf{1\%}}{\rightleftharpoons}} H^+ + \mathbf{HCO_{3^-}}$$

- ***Base:*** A molecule that will combine with $H^+$ to remove them from solution, i.e. $H^+$ acceptor.

Again it may be strong or weak according to the degree of dissociation:

a) Strong Base:

$$\mathbf{NaOH} \xrightarrow{\mathbf{100\%}} \mathbf{Na^+ + OH^-}$$

$$\mathbf{NH_4OH} \xrightarrow{\mathbf{1\%}} \underline{\mathbf{NH_4^+ + OH^-}}$$

- Free $H^+$ concentration in ECF is very low. It averages about 0.00004 mmol/L (40 nmol), compared to the plasma $Na^+$ concentration of 140 mmol/L.
- The $H^+$ concentration should be kept constant so as to keep the normal activity of many enzymes.
- $H^+$ concentration is kept constant by a balance between gain and output.

- **Sources of $H^+$: -**

*1- <u>Ingested:</u>* some free $H^+$ is ingested in food we eat.

2- *<u>Metabolism of food:</u>*

*a) Metabolism of carbohydrates:*

* The degradation of carbohydrates can generate as mush as 12.000 - 20.000 mmol of $H^+$ (volatile acid) each day:

- Oxygen in the cell combines with carbohydrates to form energy and leads to generation of $CO_2$ and $H_2O$.

- The $CO_2$ and $H_2O$ diffuse into the RBCs that supplied the oxygen. In presence of carbonic anhydrase (CA) the $CO_2$ and $H_2O$ are reversibly converted to $H^+$ and $HCO_3^-$.

$$H_2O + CO_2 \xrightarrow{CA} H_2CO_3 \rightarrow H^+ + HCO3^-$$

b) *Metabolism of proteins and lipids:* Many proteins and lipids contain sulphate and phosphate which are metabolized to H2S04 and $H_3P04$ (fixed acids). About 40 - 60 mmol of fixed acids may be produced from protein metabolism each day.

c) *Lactic acid accumulation in the muscle and ECF* when inadequate supplies of $O_2$ are delivered to muscle as in severe muscular exercise.

*d) Ketoacids* (aceto-acetic and β-hydroxy buteric acid) are produced when there is increased metabolism of fat with lack of insulin in diabetes mellitus.

The total amount of $H^+$ contained the ECF is very small compared to the amount produced everyday.

pH: The $H^+$ concentration is expressed by pH which is the minus log to base 10 of $H^+$ concentration.

pH = $- \text{Log}_{10} [H^+]$

pH of ECF = $- \text{Log}_{10} 0.00004$ = 7.4

- It's slightly alkaline.
- Life is compatible within narrow range of pH; between 7.35-7.45
- Death occurs if the pH falls below 6.8 or rises above 8.0

- **Regulation of Acid - Base Balance:**

There are three major systems involved in the regulation of $H^+$ concentration (pH):

1) *The buffer systems:* minimize the change in free $H^+$ concentration.

2) *The respiratory system:* eliminate's $H^+$ derived from $CO_2$.

3) *The kidneys:* excrete the fixed acids and restores the ECF buffers.

## ***Buffer Systems***

- A Buffer is a molecule that combines with or releases $H^+$
- It is composed of weak acid and salt of its conjugate base.

• There are many buffers in the body. The combination of all buffers determines the free $H^+$ concentration.

◆ **Relation between pH and the ratio of concentration of the buffer members.**

It is expressed by: *Henderson-Hasselbalch equation:*

$$\textbf{pH of a buffer} = \textbf{pK} + \log_{10}\frac{[\textbf{Salt}]}{(\textbf{Acid}]}$$

• *Where:*

pK: dissociation constant.

When Henderson-Hasselbalch equation is applied to the bicarbonate-carbonic acid buffer:

$[HCO_3^-]$ = 24 mmol/L

$[H_2CO_3]$ = $PCO_2$ x solubility co-efficient. = 40 x 0.03 .

pK = 6.1

$$\therefore \text{pH of arterial blood} = 6.1 + \log_{10}\frac{\mathbf{HCO_3^-}}{H_2\mathbf{CO_3}}$$

$$= 6.1 + \log_{10}\frac{24}{0.\mathbf{03 \times 40}}$$

$$= 6.1 + \log \frac{20}{1}$$

$$= 6.1 + 1.3 = 7.4$$

* Henderson-Hasselbalch equation is applied to any buffer if its pK is known and the concentrations of its buffer members are known.

- **The effectiveness the buffer depends on:**

a) Amount of the buffer pair.

b) pK of the buffer system: The buffer is most effective when its pH = pK. The nearer the pK to the pH of ECF the more is the effective of the buffer.

- **Role of buffers in regulation of acid-base balance:**

Buffers act immediately to trap $H^+$ temporarily until respiratory and renal mechanisms act. They only minimize the change in $H^+$concentration.

- **Types of buffer systems:**

1. Bicarbonate buffer system:

$$\frac{H_2CO_3}{BHCO_3} \quad (B = Na^+ or\ K^+)$$

2. Phosphate buffer system:

$$\frac{BH_2PO_4}{B_2HPO4}$$

3. Protein buffer system:

a) Plasma proteins.

b) Hemoglobin.

c) Tissue proteins.

- **Bicarbonate Buffer:**

*** Physiological Importance of Bicarbonate Buffer:**

1. Its components can be physiologically controlled:

$[HCO_3^-]$ is regulated by the kidneys.

$[H_2CO_3]$ is regulated by the respiratory system.

Therefore, it is very effective buffer.

2. Its pK 6.1 is far from the pH of the blood.

3. Its amount is not large 24 mmol/L.

4. Changes in pH that result from an alteration in either $HCO_3^-$ concentration or $PCO_2$ can be corrected by changing the other variable to preserve the buffer ratio.

5. Factors affecting the $HCO_3^-$ concentration give rise to metabolic acidosis or alkalosis while factors affecting $PCO_2$ will give rise to respiratory acidosis or alkalosis.

- **Haemoglobin Buffer:**

**Physiological Importance:**

1. It plays an important role in buffering $CO_2$.

2. High buffering capacity: It has 6 times the buffering capacity of all plasma proteins, as it is present in high amounts. There are about 700 gm of hemoglobin in the blood of an adult person. Deoxyhemoglobin is better buffer than oxyhaemoglobin.

- **Buffering of $CO_2$:**
  - $CO_2$ is produced at a rate of about 20.000 mmol per day which represents 20.000 mmol of $H^+$. Therefore, continual removal of C02 from the blood is necessary for normal $H^+$ balance.
  - Haemoglobin carries $O_2$ in the RBC from the lungs to the tissue cells.
  - As shown in (Fig. 8-1) the $O_2$ dissociates from the haemoglobin and diffuses down its concentration gradient into the tissue cells, where it is metabolized into energy and $CO_2$.

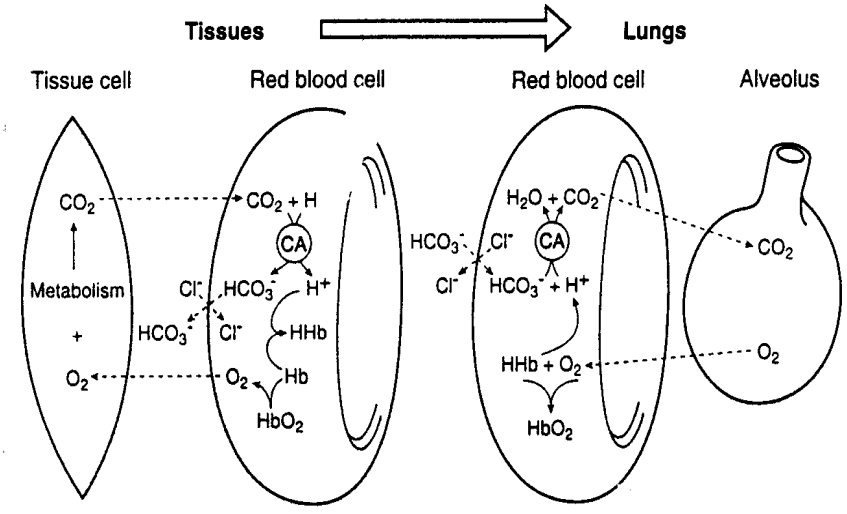


**Fig. (8-1):**
**Mechanism of Haemoglobin buffe $H^+$ generated in the tissues from metab**

- The $CO_2$ diffuses from the tissue cells into the RBC, where it combines with $H_2O$ in the presence of carbonic anhydrase enzyme to form $H_2CO_3$ which dissociate into $H^+$ and $HCO_3^-$.
- The $H^+$ combines with the deoxygenated hemoglobin where it is buffered and thus the change in free $H^+$ is minimized.
- The $HCO_3$ formed in the RBC diffuses into the plasma, and to maintain electrical neutrality, $Cl^-$ diffuses into the RBC (Chloride shift phenomenon).
- After the RBC is carried to the lungs, the process is reversed.
- <u>In the alveoli:</u>

The high $O_2$ causes its diffusion into the RBC, where it oxygenates the hemoglobin and displaces the $H^+$. The $H^+$ then combines with $HCO_3^-$that diffuses into the RBC from the plasma to form $CO_2$ and $H_2O$, The high $CO_2$ concentration in the RBC causes diffusion of $CO_2$ into the alveoli where it is expired into the air.

- The amount of $H^+$ that can be buffered is dependent on the amount of hemoglobin in the blood. The decrease in haemoglobin concentration that occurs in many patients with chronic renal failure may contribute to the acidosis seen in those patients.

- **Phosphate Buffer:**
  - It is a mixture of basic phosphate $HPO_4^{--}$ and acid phosphate $H_2PO_4^-$.
  - Physiological Importance;

1) lt is not a strong buffer extracellularly as its concentration is low (about 1 mmol/L).

2) It is an important buffer:

a. Intracellularly, due to its high concentration.

b. In the tubular fluid particularly in the distal convoluted tubule.

3) Its pK (6.8) is near to that of the plasma pH.

***N.B:*** • Intracellular buffers are mainly proteinate and organic phosphate. They can backup extracellular buffers as extracellular $H^+$ can exchange with $Na^+$, $K^+$, $Ca^+$ or $Mg^+$

• Prolonged metabolic acidosis depletes cells of K+ and bones of Ca++.

• The capacity of intracellular buffers is similar to that of extracellular buffers but the exchange between H+ and intracellular K+ or Na+ is much slower taking hours because of the limited permeability of the membrane to H+.

## *Respiratory Regulation of Body Fluids pH*

-The respiratory control of pH is done through controlling of the blood $PCO_2$.

- A decrease in $PCO_2$, in cases of rapid ventilation, will reduce $H^+$ concentration and hence raise pH according to Hasselbalch-equation for the bicarbonate buffer:

$$pH = 6.1 + \text{Log} \frac{[HCO3^-]}{\downarrow PCO_2 \text{ x } 0.03}$$

- On the other hand, a decrease in pulmonary ventilation results in an increase in $PCO_2$ and $H^+$ concentration with consequent drop in pH.

### ◆ *Mechanism of Respiratory Control of pH:*

**1. An increase in $H^+$ concentration (in metabolic acidosis).**

- It stimulates the respiratory centers through the peripheral chemoreceptors. Hyperventilation eliminates $CO_2$ and therefore the carbonic acid and $H^+$ concentration decrease.
- To illustrate this, let us consider an example when 10 mmol/L of acid is added to the system.

$$10\ HCl + 26\ Na\ HCO \rightarrow 10\ NaCl + 10\ H_2CO_3 + 16\ NaHCO_3.$$

- The above reaction indicates that the system gains 10 mmol/L carbonic acid and that the bicarbonate decreases by 10 mmol/L.

In absence of respiratory control, there will be serious deviation from the normal.

* *According to Henderson-Hasselbalch equation:*

$$pH = 6.1 + \log \frac{20}{1.2+10} = 6.1 + \log \frac{10}{11.2}$$

$$= 6.1 + 0.15 = 6.25 \text{ (Highly acidic)}$$

This pH is incompatible with life.

- It is the respiratory system, which prevent this from happening.
- Hyperventilation will decrease quickly the $PCO_2$ and the carbonic acid falls as follows:

$$pH = 6.1 + \text{Log} \frac{16}{1.0}$$

$$= 6.1 + 1.2 = 7.3$$

The correction of the blood pH is incomplete but it is compatible with life. Final correction is brought about by the kidney.

**2. A decrease in $H^+$Concentration below normal (in metabolic alkalosis):**

- The respiratory centre becomes depressed. $CO_2$ retention increase $H^+$ concentration back toward normal.

* *Control Effectiveness of the Respiratory Control:*

• The respiratory system can return $[H^+]$ and pH about two-thirds of the way back toward normal within a few minutes after a sudden disturbance of acid-base balance.

It takes 1-12 minutes to make acute adjustments in pH.

• The buffering power of the respiratory control is 1 - 2 times as all the chemical buffers combined.

• The respiratory control of the plasma pH has limited ability, because the changes in $PCO_2$ have opposite effects on respiration.

### *Renal Control of Acid - Base Balance*

When the respiratory system fails to completely restore $[H^+]$ to normal, the kidneys are capable of bringing it back toward the normal within 12-24 hours in most cases. The renal control of acid-base balance is the most efficient and most powerful buffer mechanism. (See $H^+$ secretion and $HCO_3^-$ reabsorption by renal tubule).

### *Acid - Base disturbances*

The normal pH of the arterial blood is 7.4 and is represented by a plasma $H^+$ concentration of 40 nmol/L. This is an alkaline condition since pure $H_2O$ is neutral and has a pH of 7.0. In a study of the acid - base disturbance, the state of acidity or alkalinity is referenced to the normal condition.

**Types of acid - base disturbances:**

Acidosis : Arterial pH is below 7.4.

Alkalosis: Arterial pH is above 7.4.

From Henderson - Hasselbalch equation: pH depends upon the ratio

$$\frac{[HCO_{3-}]}{PCO_2}$$

Accordingly, the disturbance may be:

**Respiratory:** The primary change is in $PCO_2$:

a) Respiratory acidosis: An increase in $PCO_2$.

b) Respiratory alkalosis: A decrease in $PCO_2$.

**Metabolic:** The abnormality of pH results from a change in $[HCO_3'^-]$:

a) Metabolic acidosis: decrease in $[HCO_3^-]$

b) Metabolic alkalosis: increase in $[HCO_3^-]$

**Compensation in acid - base disturbance:**

• Any acid - base disturbance caused primarily by one system results in compensation by the complementary system, e.g. in respiratory acidosis: The primary change is an increase in arterial $PCO_2$. The renal response is increase $H^+$ secretion and generation of $HCO_3^-$. The increase in plasma $HCO_3^-$ concentration returns the $H^+$ concentration towards normal.

• Compensation restores the pH towards normal even though $HCO_3^-$ concentration and $PCO_2$ are still disturbed.

**Respiratory acidosis:** It is characterized by: arterial blood pH less than 7.4.

Increased arterial $PCO_2$ more than 44 mmHg. $\frac{[\ \mathbf{HCO_{3-}}]}{\uparrow \mathbf{PCO_2}}$

**** Causes:-***

1. Depression of the respiratory centre by narcotics or excess sedation.
2. Air way obstruction: emphysema - bronchial asthma - asphyxia.
3. Paralysis of the respiratory muscles.

**Renal compensation:**

* Increased the plasma $HCO_3^-$ concentration thus the ratio $\frac{[\mathbf{HCO_{3-}}]}{\mathbf{PCO_2}}$ is constant.

* The increased $PCO_2$ acts as a stimulus to increase the formation of $H^+$ and $HCO_3^-$ from $CO_2 + H_2O$ in the renal tubular cells. The renal $H^+$ is secreted and the new $HCO_3^-$ is returned to the plasma.

**Respiratory alkalosis: It is characterized by:**

1) Arterial blood pH higher than 7.4.

2) Decreased arterial $PCO_2$ $\frac{[\mathbf{HCO_{3-}}]}{\downarrow \mathbf{PCO_2}}$

* *Causes:*

1. Respiratory response to high altitudes.

2. Psychological dyspnea and anxiety.

3. Fevers.

4. Early in exercise.

**Compensation:**

The kidneys decrease plasma [$HCO_3^-$]:

* Decrease reabsorption of the filtered $HCO_3^-$

* The decreased $CO_2$ decreases the generation of $H^+$ and $HCO_3^-$ by the tubular epithelial cells.

**Metabolic acidosis:**

It is characterized by:

a) Arterial blood pH is less then 7.4.

b) Decreased plasma [$HCO_3^-$].

*** *Causes:***

1. Excess production of fixed acids:

a) Diabetic ketoacidosis: addition of acetoacetate and B-hydroxybutrate to the blood.

b) Shock: anaerobic production of lactic acid.

c) Aspirin poisoning ➔ Salicylic acid.

d) Methanol poisoning ➔ formic acid.

2. Decreased elimination of fixed acids due to impaired excretion by the kidney e.g. renal failure.

3. Loss of $HCO_3^-$:

a) Prolonged or severe diarrhea. b) Pancreatic fistula.

c) Addison's disease.

**Respiratory compensation:**

• Increased $H^+$ concentration is a very potent stimulus to increase ventilation via the peripheral chemoreceptors. Increased ventilation rapidly lowers arterial $PCO_2$ and returns [$H^+$ ] toward normal.

• However, increased ventilation is insufficient to return the plasma [$H^+$] to normal and metabolic acidosis with respiratory compensation results.

• **Renal correction**: restoration of the plasma [$HCO_3^-$] to normal by increasing $HCO_3^-$generation by the kidney.

**Metabolic alkalosis:**

It is characterized by:

1. Rise of arterial plasma pH above 7.4.

2. Increased plasma [$HCO_3^-$].

* *Causes:*

An increase in plasma [$HCO_3^-$] due to:

1) Persistent vomiting:

Normally, when $H^+$ is secreted into the stomach lumen, $HCO_3^-$ generated is added to the blood. In persistent vomiting: $H^+$ and $Cl^-$ are lost in the vomitus and $HCO_3^-$ is added to the plasma.

2) Excess intake of alkali to treat peptic ulcer.

3) Cushing syndrome.

4) Conn's syndrome. { $K^+$ leaves the cells in exchange with $H^+$ ➔ [$HCO_3^-$] }

5) Diuretics: except carbonic anhydrase inhibitors.

**Respiratory compensation:**

Respiratory centres are inhibited by decreased [$H^+$].

* Hypoventilation elevates arterial $PCO_2$.

pH returns toward normal. However, increased $PCO_2$ is a very potent

stimulus to increase ventilation and thus $PCO_2$ only slightly increases. Thus, the respiratory component for metabolic alkalosis is not nearly so powerful as the respiratory component for metabolic acidosis.

**Renal correction:**

Decreased $HCO_3^-$ reabsorption by the renal tubule and increased loss of $HCO_3^-$ in urine to lower plasma $HCO_3^-$.

***Commonly Used Equations in Renal Physiology***

| Name | Equation | Units | Comments |
|---|---|---|---|
| **Clearance** | $C_x = \frac{[U]_x V}{[P]_x}$ | ml/ min | X is any substance |
| **Glomerular filtration rate** | $\mathbf{GRF} = \frac{[U]_{\mathbf{Inulin}} V}{[P]_{\mathbf{Inulin}}}$ | ml/ min | Equals $C_{inuiin}$ |
| **Estimated Glomerular filtration rate** | $GFR = \frac{(140\text{-}Age) \times Weight\ (Kg)}{P_{cr} \times 72}$ | ml/ min | For woman,it is multiplied by 0.85 |
| **Effective renal plasma flow** | $\mathbf{Effective\ RPF} = \frac{[U]_{\mathbf{PAH}} V}{[P]_{\mathbf{PAH}}}$ | ml/ min | Underestimates RPF by 10% Equals $C_{PAH}$ |
| **Renal plasma flow** | $\mathbf{PRF} = \frac{[U]_{\mathbf{PAH}} V}{[\mathbf{RA}]_{\mathbf{PAH}} - [\mathbf{RV}]_{\mathbf{PAH}}}$ | ml/min | |
| **Renal blood flow** | $\mathbf{RBF} = \frac{\mathbf{RBF}}{\mathbf{100 - HV}} \mathbf{x\ 100}$ | ml/ min | HV is fraction of blood volume that is RBC's. |

| | | | |
|---|---|---|---|
| **Filtration fraction** | $\mathbf{F\ F = \frac{GFR}{RPF}}$ | None | |
| **Filtration load** | $\mathbf{Filtered\ Load = GFR\ x\ [P]_X}$ | mg/ | |
| **Excretion rate** | $\mathbf{Excretion = V\ x\ [U]_X}$ | mg/ | |
| **Reabsorption or secretion rate** | *Reabsorption or secretion = filtered load - excretion* | mg/ min | If positive, net reabsorption If negative, net |

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